Test reliability is critically important to molecular epidemiology: an example from studies of human papillomavirus infection and cervical neoplasia

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Abstract: To demonstrate that it is critically important to achieve excellent test reliability before conducting full-scale molecular epidemiological studies, data were compared from two consecutive case-control studies of human papillomavirus (HPV) infection and cervical intraepithelial neoplasia. The major methodological difference between the two studies was the much greater reliability of the HPV test used in the second study. Although the first study used an assay considered state-of-the-art at that time, mediocre test reliability led to (a) a weakened association between HPV and risk of cervical intraepithelial neoplasia, (b) a weakened association between known risk factors for cervical intraepithelial neoplasia and HPV prevalence, (c) failure to demonstrate that HPV infection explains the known risk factors for cervical intraepithelial neoplasia, and (d) a marked reduction in the estimated proportion of cervical intraepithelial neoplasia attributable to HPV infection. With an improved assay, the second study strongly supported the idea that HPV infection is an intermediate end point explaining the known epidemiology of cervical intraepithelial neoplasia. Based on this experience and supportive theoretical considerations, we recommend that researchers optimize the reliability of innovative assays before application to full-scale molecular epidemiological projects.